Atrial electromechanical sequence in normal subjects and patients with DDD pacemakers

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Abstract

***Objective*—To assess the effect of right atrial appendage pacing on atrial electromechanical interrelations in patients with DDD pacemakers.**

***Design*—Prospective study by M mode echocardiogram, Doppler echocardiogram, and apexcardiogram, along with electrocardiogram and phonocardiogram.**

***Setting*—Tertiary cardiac referral centre.**

***Patients*—20 patients with DDD pacemakers and 20 age matched normal controls.**

***Results*—Age, RR interval, atrial size, left ventricular size, and fractional shortening were similar in the two groups. Atrial electromechanical delay (the time from the onset of P wave or atrial pacing spike on ECG to the onset of atrial contraction on M mode echogram) was 68 (SD 7) ms at the lateral site of right atrium, 82 (9) ms at the central fibrous body, 93 (11) ms at the lateral site of left atrium in normals. In patients with DDD pacing, however, this delay increased to 85 (22) ms, 117 (23) ms, and 138 (25) ms respectively (all $P < 0.01$). Interatrial mechanical delay (the time from the onset of right atrial motion to the onset of the left) increased from 25 (6) ms in normal controls to 53 (18) ms in patients ($P < 0.01$). Intra-atrial mechanical dispersion (the time from the earliest to the latest onset of regional atrial motion around the atrioventricular ring) in the right atrium increased from 6 (2) ms in normals to 19 (2) ms in patients ($P < 0.01$), but it remained unchanged in the left atrium (6 (2) ms in normal controls *v* 7 (2) ms in patients, $P > 0.05$). Peak atrial shortening rate was not different between the two groups. Differences of atrial electromechanical activity between the two groups were also reflected on Doppler echocardiogram and apexcardiogram.**

***Conclusions*—Right atrial appendage pacing disturbs the normal coordinate sequence of right atrial mechanical activity and leads to a striking and variable increase in intra-atrial conduction time as well as in interatrial conduction time. Left atrial contraction remains synchronous although the timing of the start of its contraction was delayed. These values can be determined in individual patients to allow optimal setting of DDD pacemakers.**

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Dual chamber pacemakers have been used clinically for more than 20 years.[1] They were conceived with the idea of maintaining atrioventricular (A-V) synchrony and atrial systolic function, and of providing a physiological rate response in patients with normal sinus node function and A-V block. For these reasons, dual chamber pacemakers, especially of the DDD or DDDR type, have been described as "physiological", and are considered superior to conventional VVI pacing.[2,3] However, pacing the right atrial appendage, the usual site for the atrial lead, is known to delay left atrial contraction, which may prolong the left heart mechanical A-V interval and thus affect left ventricular function.[4–6] We therefore undertook this detailed study of the electromechanical effects of right atrial appendage pacing using a series of non-invasive techniques, in order to clarify underlying mechanisms.

Methods

PATIENTS

We studied 36 patients with DDD pacemakers implanted, in whom the atrial electrode tip was positioned in the right atrial appendage. In 20, complete data were recorded, and these form the study group. Eight patients had complete A-V block or Mobitz type II second degree A-V block, eight had sick sinus syndrome, and four had sinus bradycardia. Underlying coronary artery disease was also present in three patients, and aortic valve disease in one patient. None was receiving drugs known to influence cardiac electrophysiology. Twenty age matched normals were used as controls, in whom there was no clinical, electrocardiographic (ECG), radiographic, or echocardiographic evidence of heart disease.

ECHOCARDIOGRAPHY

A standardised series of M mode echocardiograms, guided from the cross sectional display, was recorded from right and left A-V rings with the patients in left lateral position, by a 2·5 MHz phased array transducer with a Hewlett Packard Sonos 1000 system. Echocardiograms were recorded photographically at a paper speed of 100 mm/s, with simultaneous lead II ECG showing a clear P wave or

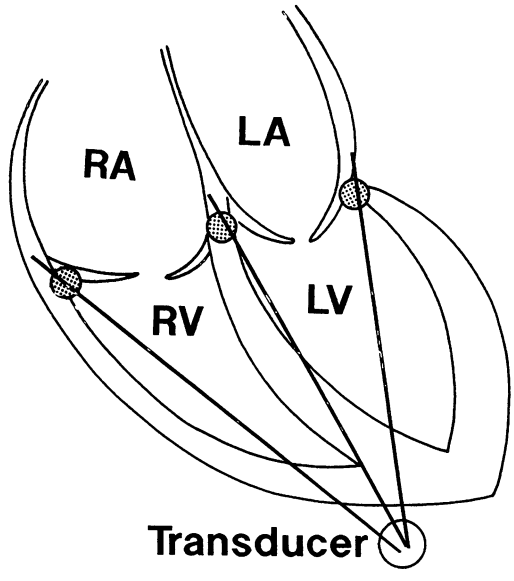

Figure 1 Diagram of apical four chamber cross sectional view showing the M mode cursor positioned through the lateral tricuspid ring, the central fibrous body, and the lateral mitral ring.

atrial pacing spike, along with a phonocardiogram. Motion of the A-V rings during the cardiac cycle was obtained with the M mode cursor directed from the apical four chamber view.[7] The cursor was longitudinally placed through the anterior, lateral, and posterior sites of right and left A-V rings and through the central fibrous body (figs 1 and 2). At each site, the beam was oriented so that it was parallel to the longitudinal component of the A-V ring motion. In addition, a standard minor axis left ventricular M mode echocardiogram, pulsed Doppler records of transmitral and transtricuspid blood flow, and a left ventricular apexcardiogram (ACG) were also recorded. The M mode echograms of the A-V rings were digitised[8] to quantify the extent and velocity of movement (fig 2).

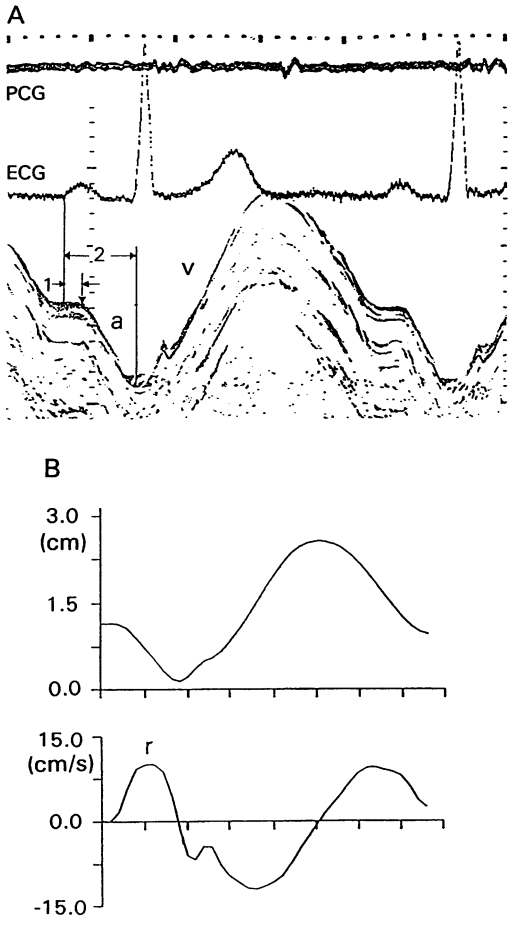

Figure 2 (A) M mode echocardiogram at the lateral site of tricuspid ring in a normal subject. Movements of the atrioventricular ring represent mechanical activity of right atrium (a) and right ventricle (v). (B) The upper panel shows the digitised plot of the trace. The lower panel shows the peak atrial shortening rate (r). ECG, electrocardiogram; PCG, phonocardiogram; 1, atrial electromechanical delay, it was measured from the onset of the P wave on ECG to the onset of atrial shortening; 2, the time interval from the onset of the P wave on ECG to the maximum atrial shortening amplitude

A typical M mode echocardiogram of the right A-V ring is shown in fig 2. During ventricular systole the A-V ring moves towards the apex of the ventricle. During ventricular diastole, there is a rapid movement in the reverse direction corresponding to ventricular early diastole. There is in addition a clear second reverse movement which corresponds to atrial systole. During atrial systole, movements at the different sites of A-V rings reflect mechanical activity of different regions of the two atria, while movement of central fibrous body (CFB) reflects mechanical activity of the interatrial septum.[9]

The following measurements were made from these records:

On A-V ring echograms:

(1) Regional atrial electromechanical delay: This interval was measured from the onset of the P wave or atrial pacing spike on ECG to the onset of atrial mechanical activity phase of A-V ring motion (fig 2). Electromechanical delay was measured at each of the seven sites.

(2) The peak atrial shortening rate, from the corresponding digitised trace (fig 2).

(3) The time interval from the onset of the P wave or atrial pacing spike to the maximal atrial shortening amplitude (P maximum shortening) (fig 2).

On the Doppler record and apexcardiogram:

(1) The time interval from the onset of the P wave or atrial pacing spike to the onset of the A wave on transmitral and transtricuspid flow (P onset of A wave).

(2) A wave peak velocity on transmitral and transtricuspid blood flow.

(3) The time interval from the onset of the P wave or atrial pacing spike to the onset of the A wave on the apexcardiogram (P onset of A wave on ACG).

We also measured left ventricular end diastolic and end systolic dimensions and fractional shortening, and left atrial dimension on the standard transverse M mode echocardiogram.

In the normal group, the onset of P wave on ECG was derived by determining the PR interval on a standard 12 leads ECG, using Hewlett Packard pagewriter software. Individual measurements were made from the Q wave of the ECG, which was a more reproducible landmark, and the computed PR interval added. In the DDD pacing group, only the heart beats with both atrial and ventricular pacing were used.

From these measurements, the following quantities were calculated:

(1) Interatrial mechanical delay: the time interval from the onset of atrial mechanical motion at the lateral site of the right A-V ring to that of the lateral site of the left.

(2) Intra-atrial mechanical dispersion. This was defined as the time difference from the earliest to the latest onset of regional atrial motion among the three sites on each atrium.

It represents the spread over time of the onset of mechanical activity in each atrium.

(3) The time delay from the onset of mechanical atrial contraction at the A-V ring to the onset of the A wave on the two Doppler records or on the apexcardiogram. We measured the time from the onset of atrial contraction at the lateral site of left side A-V ring to the onset of A wave on transmitral flow and on ACG, and the time from the onset of atrial contraction at the lateral site of right side A-V ring to the onset of A wave on transtricuspid flow.

REPRODUCIBILITY

To assess reproducibility of the variables on which our major conclusions depend, electromechanical intervals in 18 patients were measured by two blinded observers. Variables included atrial electromechanical delay at the seven sites of A-V ring on M mode, and the time intervals on Doppler and apexcardiogram.

DATA ANALYSIS

The average values were taken from three successive beats. They were expressed as mean (SD) for group measurements. Paired and unpaired Student t tests were used as appropriate. $P < 0.05$ was considered to be statistically significant. Reproducibility was assessed from root mean square difference of duplicate determinations.

Results

GENERAL DATA

There were no significant differences between two groups with regard to age, RR interval, left ventricular cavity size, fractional shortening, and left atrial dimension (table 1).

NORMAL SUBJECTS

The onset of mechanical wall motion in each atrium was effectively synchronous, that of the right atrium following approximately 68 ms after the onset of the P wave and that of the left atrium approximately 93 ms (table 2). Interatrial mechanical delay was 25 (6) ms, and intra-atrial mechanical dispersion was 6 (2) ms for both atria. In spite of the consistent delay in the onset of shortening on the left side, the timing of maximum shortening was synchronous in the two atria, occurring about 185 ms after the start of the P wave (table 3). Peak shortening rate was rather lower on the left than the right (table 3), compatible with smaller overall amplitude of motion.

Other electromechanical intervals on the Doppler and ACG corresponded to that on M mode (table 4). The onset of A wave on the Doppler and apexcardiogram were both consistently delayed with respect to that directly measured from A-V ring motion, by 19 ms for the mitral, 27 ms for the tricuspid Doppler, and 13 ms for apexcardiogram (table 5).

DDD PACING GROUP

Electromechanical delay was prolonged (table

Table 1 General data. Values are mean (SD)

Index	*Normal controls (n = 20)*	*Patients (n = 20)*
Age (years)	57 (18)	65 (11)
Sex (male:female)	11:9	12:8
P-R interval or A-V delay (ms)	175 (22)	189 (37)
R-R interval (ms)	878 (117)	812 (91)
LA dimension (mm)	32 (6)	31 (6)
LVEDD (mm)	50 (4)	51 (10)
LVESD (mm)	34 (5)	36 (9)
FS (%)	33 (6)	30 (7)

LA, left atrium; LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimension; FS, left ventricular fractional shortening. No significant difference between the two groups.

Table 2 Atrial electromechanical delay. Values are mean (SD)

Site	*Normal controls (n = 20)*	*Patients (n = 20)*
R anterior (ms)	67 (7)	79 (28)
R lateral (ms)	68 (7)	†85 (22) *
R posterior (ms)	69 (7)	†96 (25) *
CFB (ms)	82 (9)	†117 (23)
L anterior (ms)	92 (10)	†136 (25)
L lateral (ms)	93 (11)	†138 (25)
L posterior (ms)	92 (11)	†136 (23)

R, right atrium; L, left atrium; CFB, central fibrous body.
†$P < 0.01$ *v* normal controls; *$P < 0.01$ by intragroup comparison.

Table 3 Atrial electromechanical measurements on M mode echogram. Values are mean (SD)

	P to maximum shortening (ms)		*Peak shortening rate (cm/s)*	
	Normal controls	*Patients*	*Normal controls*	*Patients*
Site	*(n = 20)*	*(n = 20)*	*(n = 20)*	*(n = 20)*
R anterior	188 (16)	†223 (23)	8·4 (2·1)	8·1 (2·9)
R lateral	188 (16)	†220 (26)	9·4 (2·3)	10·5 (3·3)
R posterior	186 (16)	†220 (24)	8·6 (2·6)	8·9 (2·8)
CFB	184 (19)	†214 (24)	6·2 (1·7)*	6·6 (1·6)*
L anterior	182 (19)	†220 (26)	6·3 (1·5)	6·8 (1·5)
L lateral	183 (19)	†220 (24)	6·5 (1·5) *	7·3 (1·7) *
L posterior	184 (19)	†221 (23)	6·3 (1·7)	7·1 (1·5)

R, right atrium; L, left atrium; CFB, central fibrous body.
†$P < 0.01$ *v* normal controls; *$P < 0.01$ *v* right side in intragroup comparison.

Table 4 Doppler and apexcardiogram. Values are mean (SD)

Index	*Normal controls (n = 20)*	*Patients (n = 20)*
Transmitral flow		
P to onset of A wave (ms)	112 (16)	131 (21)†
A wave peak velocity (m/s)	0·57 (0·17)	0·73 (0·20)†
Transtricuspid flow		
P to onset of A wave (ms)	95 (14)	102 (23)
A wave peak velocity (m/s)	0·34 (0·08)	0·42 (0·15)
Apexcardiogram		
P to onset of A wave (ms)	106 (16)	149 (20)†

†$P < 0.01$ *v* normal controls.

Table 5 Atrial interrelations. Values are mean (SD)

Index	*Normal controls (n = 20)*	*Patients (n = 20)*
Time from onset of left atrial contraction to onset of A wave on MV (ms)	19 (12)	−7 (12)†
Time from onset of right atrial contraction to onset of A wave on TV (ms)	27 (15)	17 (21)
Time from onset of left atrial contraction to onset of A wave on ACG (ms)	13 (10)	11 (11)

†$P < 0.01$ *v* normals controls.
MV, mitral valve; TV, tricuspid valve; ACG, apexcardiogram.

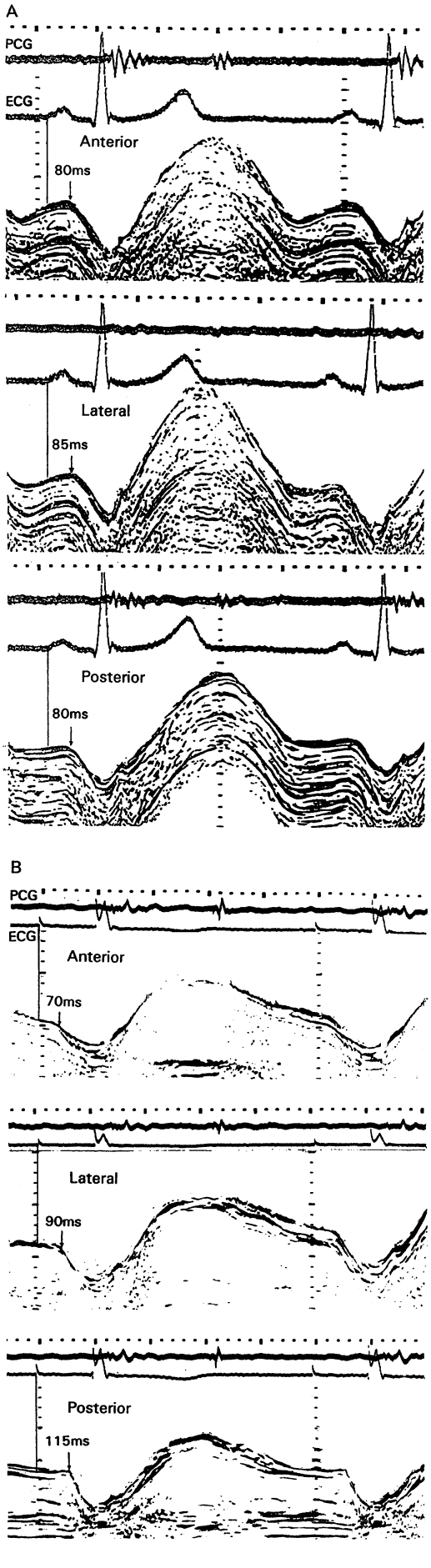

Figure 3 (A) M mode echocardiograms at the anterior, lateral, and posterior sites of tricuspid ring in a normal subject, which show that the timing of right atrial shortening at these three sites is synchronous, and the range of atrial electromechanical delay is 80–85 ms at the three sites. (B) M mode echocardiograms at the anterior, lateral, and posterior sites of tricuspid ring in a patient with DDD pacemaker, which show that the timing of right atrial shortening at these three sites is asynchronous, and the range of atrial electromechanical delay is 70–115 ms at the three sites. Abbreviations as in fig 2.

2), and right atrial mechanical dispersion considerably increased to 19 (2) ms ($P < 0.01$ compared to normals). Furthermore, a characteristic sequence appeared, with atrial movement of the A-V ring beginning at the right side, followed by the anterior, lateral, and posterior walls (fig 3), and finally the septum and left side (table 2). The mean value of interatrial mechanical delay was approximately double the normal value (25 (6) ms in normals versus 53 (18) ms in pacing group, $P < 0.01$). In spite of this, the contraction pattern of the left atrium remained coordinate, though with some increase in scatter among patients (table 2), so that the overall value for mechanical dispersion was not significantly different from normals (6 (2) ms in normals versus 7 (2) ms in pacing group, $P > 0.05$).

The onset of the A wave on the Doppler and apexcardiogram were also delayed with respect to normals, by 7 ms for the transtricuspid, 19 ms for the transmitral Doppler, and 43 ms for the apexcardiogram (table 4). However, the intervals from the onset of atrial mechanical shortening to the onset of A wave were similar to those in the normal controls, apart from what appeared to be the premature onset of the A wave on the transmitral Doppler (table 5). Once atrial contraction began, the timing of maximum shortening was synchronous not only within but also between the two atria, and peak atrial shortening rate did not differ significantly from that in the normal controls (table 3).

REPRODUCIBILITY

There were no consistent differences between pairs of duplicate determinations. The range of root mean square difference was from 4·4 to 5·4 ms on M mode echogram, and from 5·2 to 7·0 ms on Doppler and apexcardiogram.

Discussion

Our technique depends on recording atrial wall movement directly rather than its indirect consequences in terms of blood flow across the A-V valves[10] and atrial pressure pattern.[11] Since electromechanical interval is unlikely to change, delay in local activation will be followed by a similar delay in the onset of shortening. Several atrial sites can be examined, and the coordination, the extent, and the velocity of local shortening assessed. This information has been correlated with Doppler and apexcardiogram, representing the overall function of the atriums.

Normal atrial wall motion is effectively synchronous, with a consistent sequence in the onset of motion involving the right atrium, the septum, and the left atrium. During right atrial appendage pacing, the contraction sequence of the right atrium became asynchronous (fig 3), starting at the anterior site of the tricuspid ring, followed by the lateral, and subsequently the posterior site, with an overall dispersion of nearly 20 ms. The indirect effects of atrial contraction with respect to the normals were also delayed. Left atrial contraction, though delayed, was as synchronous as in the normal controls.

The differences between the relative times of onset of mechanical events in sinus rhythm and atrial pacing shed light on normal and

abnormal atrial activation pathways. There is no interatrial conduction pathway analogous to the His-Purkinje system in the ventricles.[12 13] Instead, conduction occurs preferentially in regions of increased muscle thickness.[14 15] The terminal crest, between the sinus node and the pectinate muscles supporting the right A-V ring, is likely to be responsible for the coordinate onset of right atrial motion. When it is activated from the right atrial appendage, conduction velocity is much slower, and the spread of activation takes nearly 20 ms to pass around the A-V ring. By contrast, left atrial contraction is synchronous, strongly suggesting that a preferential pathway has now become involved, although the increased interatrial mechanical delay shows that the route by which the activity wave front has reached the left atrium is clearly abnormal. These findings stress a fundamental difference between preferential pathways in the atrium, to which access can be gained from the myocardium, and the His-Purkinje system of the ventricle where this is not possible.[12 13 16]

Our study clearly had limitations. The most important was that a significant number of the patients with pacemakers had a diagnosis of sinus node disease, and might thus have had intrinsic atrial disease. In suitable patients, this possibility might have been circumvented by studying the same patients before and after pacemaker insertion. However, the consistency of the effects of atrial pacing makes it most unlikely that atrial disease was responsible. We used different landmarks to assess the onset of atrial electrical activity in the two groups: the onset of the P wave is clearly not identical with the pacing artefact, so that absolute estimates of atrial electromechanical delay cannot be compared. This difference does not, of course, preclude studying dispersion of mechanical events in individual patients. Our observations of atrial mechanical activity were confined to the two A-V rings. It would obviously have been desirable to have made a more extensive study of the atriums, but we are unaware of other reproducible landmarks suitable for study by transthoracic echo. It is possible that their number might have been extended by transoesophageal echo, which allows access to the two atrial appendages.

Physiological "asynchrony" between the two atria has been well recognised for many years. The right atrial contraction has been shown to precede the left by approximately 13 ms in the dog[16] and by 20 ms in man.[11] Interatrial electrical conduction delay has been measured in man using catheters in the right atrium and coronary sinus,[17 18] normal values being 77 (8) ms with the range 62–88 ms.[17] These values are significantly greater than those of mechanical interatrial delay we obtained in our study. Obviously, this difference cannot be ascribed to any peculiarity of motion of the two A-V rings, since their relative onset of motion was directly reflected in the relative times of onset of tricuspid and mitral Doppler A waves. It seems very unlikely that the electromechanical coupling interval differs between the two atria. If the extent of left sided mechanical delay was as great as that predicted from electrical measurement, it would have profound haemodynamic consequences in that the normal left atrial contribution to left ventricular filling would not occur. The likeliest reason for the long electrical interatrial delay appears to be that left atrial potentials measured from the coronary sinus or oesophagus are significantly delayed with respect to those activating the atrial muscles which underlie left atrial contraction, while those on the right are likely to be recorded high in the atrium near the sinus node.

The methods we have described here may form the basis of an additional method of studying atrial function, and of deriving basic information about preferential conduction within the atria. This approach might be used in association with Doppler studies, to optimise pacemaker settings, and to investigate atrial function in patients with sinus node disease or following atrial surgery.

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